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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,428	06/28/2004	Eiji Sugaru	229576	7677

23460 7590 07/25/2006

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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,428	SUGARU ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-17,22-30,36,37,39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-21,31-35 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/ Election/Restrictions

Applicant's election with traverse of Group VIII (claims 18-21 and 35) and SEQ ID NO:2 in the reply filed on May 30, 2006 is acknowledged. The traversal is on the ground(s) that Groups I-XII have a common technical feature because they recite therapeutic agents that regulate the G protein-coupled receptor (GPCR) 5D. In addition, Applicant argues that searching any Group from Groups I-XII can uncover the prior art for the rest of Groups and it is not an undue search burden for the examiner to examine all the claims in Groups I-XII. This is not found persuasive because based on PCT rule, the inventions I-XII lack unity of invention. SEQ ID NO:2 is known in the art, and disclosed in WO200261087. Thus, the Invention of the Group I was found to have no special technical feature that defined the contribution over the prior art. Since the 1st claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions do not have a single inventive concept and so lack unity of invention. In addition, an undue burden isn't a criterion for restriction under lack of unity. However, upon reconsideration, claims 31-34 and 38 are rejoined to the elected Group as encompassing related subject matter and same scope of invention.

The requirement is still deemed proper and is therefore made FINAL.

The examiner has required restriction between product and process claims. Where

applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does

not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 1-40 are pending. Claims 1-17, 22-30, 36, 37, 39 and 40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 18-21, 31-35 and 38 are under examination in this office action.

Claim Objections

Claims 18-21, 31-35 and 38 are objected to as encompassing non-elected SEQ ID NO:4.

Claims 18-21, 31 and 32 are objected to under 37 CFR 1.75(c), because they depend from non-elect claims and fail to require the limitations of non-elected claims. Claims 18 and 20 depend from claim 13. Claims 19 and 21 depend from claim 16. Claim 31 depends from claim 24. Claim 32 depends from claim 27. However, claims 13, 16, 24 and 27 are non-elected claims. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-21, 31-35 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying a substance affecting signaling of SEQ ID NO:2, identifying Gαs2 subunit capable of coupling with SEQ ID NO:2 or identifying anti-GPRC5D/SEQ ID NO:2 using a screening system comprising SEQ ID NO:2 and a constitutively active form of Gαs2/Gαi2/Gα16, does not reasonably provide enablement for a method of screening for a substance having therapeutic activity against Cibophobia or lifestyle-related disease, a method of identifying any Gα subunit capable of coupling with SEQ ID NO:2 or a method of identifying any ligand for GPRC5D/SEQ ID NO:2 comprising a screening system comprising a lipid bilayer membrane comprising SEQ ID NO:2 with any modification, any receptor-binding region of G protein, any guanine-nucleotide binding region or any effector as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Claims 18-19 and 35 are directed to a method of screening for a test substance having a therapeutic activity against cibophobia/lifestyle-related disease comprising a screening system comprising a lipid bilayer membrane comprising SEQ ID NO:2, modified SEQ ID NO:2 or a combination of an ortholog of SEQ ID NO:2 and a polypeptide comprising a receptor-binding region of G protein α subunit belonging to a certain family and a guanine nucleotide-binding region of any Gα subunit. Claims 34 and 38 are directed to a method of screening for a ligand for SEQ ID NO:2, modified SEQ ID NO:2 or an ortholog of SEQ ID NO:2 comprising a screening system comprising a lipid bilayer membrane comprising SEQ ID NO:2, modified SEQ ID NO:2 or a combination of an ortholog of SEQ ID NO:2 and a polypeptide comprising a Gαs subunit and a guanine nucleotide-binding region of any Gα for screening for a substance having a therapeutic activity against cibophobia/lifestyle-related disease. The instant specification, as filed, provides no guidance or working examples as to enable one skilled in the art to how to practice the instant methods of screening therapeutic

substance for cibophobia/lifestyle-related disease using the screening system recited in the claims 13, 16, 24, and 27, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The nature of the invention is based on the data of the expression of an orphan GPCR, which the corresponding ligand is unknown, GPRC5D, in the hypothalamus of obese mouse model and the data of inhibiting the expression of GPRC5D by administration of an antisense oligo of GPRC5D to these obese model mice and subsequently resulting in increasing food intake and the level of blood glucose. Based on the results, Applicant concluded that GPRC5D is a receptor involved in the signal transduction negatively regulating the feeding behavior of the animal; and therefore, a substance inhibiting expression or function of this receptor would show a therapeutic effect on eating disorders such as cibophobia. In contrast, Applicant concludes, a substance enhancing expression or function of this receptor would show a therapeutic effect on lifestyle-related diseases including type II diabetes caused by overeating or obesity. Applicant proposed to construct several screening systems, which include a series of receptor-G protein coexpression systems comprising the polypeptide or fusion protein of SEQ ID NO:2 or modified SEQ ID NO:2, a polypeptide comprising a receptor-binding region of a G protein α subunit belonging to a certain family (Gα) and a guanine nucleotide-binding region of any Gα subunit, a GDP/GTP exchange reaction of G protein or the activity of an effector responding to G protein, in the presence or absence of a test substance. Based on the screening systems, Applicant proposed to screen for a substance having therapeutic activity against cibophobia or other lifestyle-related

diseases or screen for a ligand for SEQ ID NO:2 or a G protein α subunit capable of coupling to SEQ ID NO:2.

The art recognizes that G protein heterotrimers coupled to a GPCR encompass a Gαβγ complex. The heterotrimeric αβγ G proteins are responsible for the signal pathway of a GPCR. The Interaction of an activated GPCR with a G protein catalyzes the exchange of GTP for GDP and subsequently dissociates Gα-GTP from the Gβγ complex. The dissociated Gα–GTP and Gβγ further activates/interacts with the downstream effectors. Currently, there are 16 genes encoding for Gα subunits, 5 genes for Gβ subunits and 14 genes for Gγ subunits (Kostenis et al. Trends in Pharmacol. Sci. 2005. 26:595-602). The Gα subunit family can be categorized into four groups based on their sequence homology. They are $G_s\alpha$, $G_{i/o}\alpha$, $G_{q/11}\alpha$ and $G_{12/13}\alpha$ families. The $G_s\alpha$ family is responsible for stimulation of adenylyl cyclase and consists of $G_s\alpha$ and $G_{olf}\alpha$. The $G_{i/o}\alpha$ family is responsible for the inhibition of adenlyly cylase consist of $G_i\alpha$1-3, $G_o\alpha_{A-B}$, $G_z\alpha$, $G_t\alpha_{1-2}$ and G_{gust}. The $G_{q/11}\alpha$ family consists of $G_q\alpha$, $G_{11}\alpha$, $G_{14}\alpha$, and $G_{16}\alpha$ ($G_{15}\alpha$ is the murine orthologue of $G_{16}\alpha$) and is responsible for stimulation of phopholipase Cβ (PLC-β). The activation of $G_{12}\alpha$ and $G_{13}\alpha$ is associated with stimulation of small G-protein Rho (p.595, 2nd col. 2nd paragraph). The art recognizes that the ligands for orphan GPCR are unknown and they can be any biogenic molecules, amino acids, neurotransmitters or peptides. In addition, there are several chimeric G proteins have been proposed to be used for drug discovery. Several domains of Gs have been shown to be able to interact with GPCRs, such as C-terminal

8 amino acids, N-terminal domain, α4 helix, α4-β6 loop domain, α5 helix, α3-β5 region and the loop between the N-terminal α helix to β1 strand of GTPase domain (p.595, 2nd col. 3rd paragraph). The art does not recognize any involvement of any particular G protein complex is responsible for the signal transduction of GPRC5D/SEQ ID NO:2 or any relationship of regulating of G protein of SEQ ID NO:2 with cibophobia (fear of food or eating disorders) or lifestyle-related disease such as obesity.

In addition, the art recognizes that there are many mechanisms that have been proposed to be potentially involved in cibophobia (fear of food) or eating disorders or obesity or energy balance. For example, it has been proposed that the endocannabinoid system which consists of endocannabinoids, cannabinoid receptors, and enzymes catalyzing the synthesis/degradation of endocannabinoids, controls food uptake and energy balance (p. 585, 2nd col. 2nd paragraph. Di Marzo et al. Nat. Neurosci. 2005. 8: 585-589). The potential mechanism of the endocannabinoid system influencing food intake is by regulating the expression and activities of several hypothalamic anoretic and orexigenic mediators (p. 586, 2nd col., 2nd paragraph). It has also been proposed that obesity is linked to genetic factors (Farooqi et al. Ann. Rev. Med. 2005. 56: 443-58). For example, genetic disruption of leptin-melanocortin pathway has been linked to obesity (p. 443,abstract). Applicant shows no working example as to how SEQ ID NO:2/GPRC5D and its signaling pathway has been related to any cibophobia or eating disorders, or obesity or other lifestyle-related disease in the specification, as originally filed. Applicant provides no guidance as to how regulating G protein signaling can lead to treating cibophobia or obesity or other lifestyle-related disease. Although Applicant

discloses that the expression of GPRC5D/SEQ ID NO:2 can be identified in obesity mouse model and reducing the expression of GPRC5D/SEQ ID NO:2 by antisense against GPRC5D/SEQ ID NO:2 results in food update/increased blood glucose, Applicant fails to provide a nexus between regulating the signaling pathway of GPRC5D/SEQ ID NO:2 and treating cibophobia/eating disorders/obesity/lifestyle-related disease. While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the results of study in treating patients suffering from cibophobia or lifesylte-related disease condition in view of the total absence of support in art or in the instant specification.

Applicant's invention is predicated on the hypothesis that ligands and G protein subunit proteins interacting with GPRC5D are potentially involved in the pathogenesis of cibophobia or lifestyle-related disease. Applicant further extrapolates this result into a method of screening a test substance for treating cibophobia or other lifestyle-related disease. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine what compounds would modulate the signal transduction of GPRC5D/SEQ ID NO:2 and further test if these compounds would be useful for treating Cibophobia or any lifestyle-related disease.

To practice such a method would require knowledge of what specific signal transduction is involved in GPRC5D/SEQ ID NO:2 and what other molecules are involved in the pathogenesis of cibophobia or any lifestyle-related disease and further

screening for potential substance having therapeutic activity against cibophobia or any lifestyle-related disease. However, the instant specification provides no such information to enable one of skill in the art to practice the claimed invention in screening therapeutic substances for cibophobia or lifestyle-related disease, or feeding suppressive activity, anti-obesity activity, anti-diabetic activity or anti-hyperlipidemic activity as recited in the claims 18, 34, 35 and 38. The instant specification also fails to disclose how to determine whether a substance has a therapeutic activity in these diseases as mentioned above or how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a skilled artisan would required to perform a substantial amount of undue experimentation to resolve the potential binding ligands and understand the signal transduction mechanisms and further determine whether the specific signal transduction of GPCR5D/SEQ ID NO:2 is indeed involved in pathogenesis of cibophobia or any lifestyle-related disease. The instant specification is not enabling for screening a therapeutic substance because one can not follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

Claims 20-21 are directed to a method for identifying a G protein α subunit capable of coupling to SEQ ID NO:2, modified SEQ ID NO:2 or a orthologue of SEQ ID NO:2 comprising a screening system comprising a lipid bilayer membrane comprising SEQ ID NO:2, modified SEQ ID NO:2 or a combination of an ortholog of SEQ ID NO:2

and a polypeptide comprising a Gαs subunit and a guanine nucleotide-binding region of any Gα2 and/or an effector-interacting region and an effector. Claims 31-34 and 38 are directed to a method of identifying a ligand for SEQ ID NO: for a ligand for SEQ ID NO:2, modified SEQ ID NO:2 or an ortholog of SEQ ID NO:2 comprising a screening system comprising a lipid bilayer membrane comprising SEQ ID NO:2, modified SEQ ID NO:2 or a combination of an ortholog of SEQ ID NO:2 and a polypeptide comprising a Gαs subunit and a guanine nucleotide-binding region of any Gα2 and/or an effector-interacting region and an effector. Applicant discloses Gαs2 is a G protein subunit capable of coupling to SEQ ID NO:2 by a coexpression system comprising a constitutively active form of Gαs2 and SEQ ID NO:2 and detecting the amount of cAMP. However, as mentioned above, there are many members of Gα, Gβ and Gγ are capable of coupling to a GPCR and responsible for the signal pathway of GPCR (Kostenis et al. Trends in Pharmacol. Sci. 2005. 26:). Applicant fails to define/specify what specific conserved structures/characteristics are required for these Gα, Gβ or Gγ subunit responsible for signaling pathway of this GPRC5D/SEQ ID NO:2 in the screening system as recited in the claims 13, 16, 24, 27. Applicant is enabled for a method of identifying a specific G subunit responsible for signal pathway of SEQ ID NO:2. However, Applicant is not enabled for a screening system comprising a lipid bilayer membrane comprising any chimeric G protein subunit or any modified SEQ ID NO:2 because Applicant fails to define/specify what specific conserved/structures/characteristics that are required for polypeptides comprising any receptor-binding region of any G a subunit and any guanine nucleotide binding region of

any G α subunit and any effecter-interacting region and any effector as recited in the claims. It has been shown that any biogenic molecules/amino acids/neurotransmitters can be a ligand for an orphan GPCR (Leibmann Curr. Pharmaceutical Design. 2004: 10: 1937-1958). The reverse pharmacology approach has been used to identify the ligands for an orphan GPCR, orexin receptor (p.1945. section 4.4 orphan receptors: hundreds of putative drug target). In addition, synthetic ligands, such as receptor activated solely by synthetic ligands (RASSL) for GPCRs (Gs-coupled melanocortin-4 receptor and 5-HT4-R) have been practiced in the field for drug discovery (p. 1947, section of 4.6 High-Tech Weapons, RASSLs and TRECs). Applicant fails to provide guidance as to what regions/amino acid sequence could be/could be changed in modified SEQ ID NO:2 in order to maintain the biological activity of SEQ ID NO:2 or to promote the exchange of GTP/GDP. Applicant is enabled for the identification of an anti-GPRC5D/SEQ ID NO:2 antibody using a system comprising SEQ ID NO:2. However, Applicant fails to provide enough guidance as to enable one of skill in the art to identify any ligand for GPRC5D/SEQ ID NO:2 or modified SEQ ID NO:2 or a combination of an orthologue of SEQ ID NO:2 and a polypeptide comprising any receptor-interacting region of any G protein and any guanine nucleotide-binding region of any G protein and a polypeptide comprising any effector-interacting region and any effector with any activity. The specification does not provide any working example as to enable one of skill in the art to practice the claimed method to identify any ligand for SEQ ID NO:2 or modified SEQ ID NO:2 using other screening systems recited in claims 13, 16, 24, and 27 except the screening system comprising SEQ ID NO:2 and an constitutively active form of

Gαs2/Gαi2/Gα16. Applicant is enabled for identifying a ligand/a substance affecting Gαs2 using the screening system comprising SEQ ID NO:2 and a constitutively active form of Gαs2 and detecting the amount of cAMP to determine whether a test ligand/substance is a real ligand to activate SEQ ID NO:2 or substance affecting Gαs2. However, Applicant fails to provide guidance as to what common regions/structures/characteristics of a modified SEQ ID NO:2 are required for screening a G protein subunit or a ligand/test substance. Applicant also fails to define/specify what specific structures/characteristics are required for a receptor-binding region, a guanine nucleotide binding region or an effector-interacting region. A skilled artisan can not contemplate what specific regions/structures/characteristics of the receptor-binding region, a guanine nucleotide binding region or an effector-interacting region are in order to practice the full scope of the invention, indicating that undue experimentation is required.

Therefore, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to a method of screening for a substance having a therapeutic activity against Cibophobia or lifestyle-related disease, a method for identifying a G protein a subunit and a method of identifying a ligand for SEQ ID NO:2 comprising a screening system recited in claims 13, 16, 24, and 27.

Claims 18-21, 31-35 and 38 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 18-19 and 35 are directed to a method of screening for a test substance having a therapeutic activity against cibophobia/lifestyle-related disease comprising a screening system recited in claims 13 and 16. Claims 20-21 are directed a method for identifying a G protein α subunit capable of coupling to SEQ ID NO:2 or modified SEQ ID NO:2 comprising a screening system recited in claims 13 and 16. Claims 31-34 and 38 are directed to a method of identifying a ligand for SEQ ID NO:2 or modified SEQ ID NO:2 comprising a screening system recited in claims 24 and 27. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. Based on the instant specification, it is clear that Applicant is in possession of a screening system comprising SEQ ID NO:2, and a Gα subunit protein Gαs2, Gαi2 or Gα16. However, the claims are

drawn to not only the full length wild type of SEQ ID NO:2 and a Gαs2/Gαi2/Gα16 protein but also polypeptides of SEQ ID NO:2 with any modification, polypeptides comprising any receptor-binding region of G protein and any guanine nucleotide binding protein, polypeptides comprising any effector-interacting region and any effector activity. Thus, the claims are not limited to using proteins with a specific amino acid sequence. The specification only describes several Gα subunit proteins and effectors and fails to teach or describe any other proteins, which lacks their amino acid sequence and has any relevance to the known proteins. The claims do not require that the proteins used in the claimed methods possess any particular conserved structures/characteristics, or other disclosed distinguishing features. Thus, the claims encompass a genus of polypeptides of SEQ ID NO:2, a genus of polypeptides comprising a receptor-binding region of G protein, a genus of polypeptides comprising a guanine nucleotide binding protein, a genus of polypeptides comprising an effector-interacting region and a genus of activity of the effector. The instant specification fails to describe the entire genus of proteins which are encompassed by these claims. The only factor present in the claims is a partial structure in the form of proteins. There is not even identification of any particular portion of the structure that must be conserved. Although, Applicant describes some examples of the receptor-binding region and guanine nucleotide binding region and effector binding region in p. 31-33), Applicant fails to define/specify the common characteristics for polypeptides comprising a receptor-binding region of any G protein, and a guanine nucleotide binding region of any G protein and polypeptides comprising an effector-interacting region as recited in claims 13, 16, 18-21, 24, 27. Although

Applicant describes some examples of effector activity (see p.34-38), Applicant also fails to define/specify the common characteristics for activities of the effector as recited in claims 16, 21, 27 and 31. Applicant is able to evaluate some known effector activities in the art such as the cAMP amount/intracellular Ca^{++} or adenylyl cyclase in response to Gαs subunit, adenylyl cyclase in response to Gαi or phospholipase C (PLC) in response to Gαq. However, Applicant fails to define/specify specific characteristics that are required for effecter activities in response to specific Gα subunit. One of skill in the art cannot envision what particular characteristics/features are required for the genus of polypeptides comprising a receptor-binding region of any G protein and a guanine nucleotide binding protein of any G protein, the genus of polypeptides comprising an effector-interacting region and a genus of effector activity in order to evaluate the effects of test agents. While a genus of polypeptides is provided, there is merely a set of common properties: there is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the claimed polypeptides or effector activity encompassed: there is no guidance in the art as to what the defining characteristics of a polypeptide comprising a receptor-binding region of any G protein and a guanine nucleotide binding protein of any G protein, a polypeptide comprising an effector-interacting region and a genus of effector activity might be. Since the common characteristics/features of the polypeptides comprising a receptor-binding

region of any G protein and a guanine nucleotide binding protein of any G protein, polypeptides comprising an effector-interacting region and a genus of effector activity are unknown, a skilled artisan can not contemplate the functional correlations of the effects of test compounds, activity of effector with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins used in the claimed methods.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, a method of screening for a test substance having a therapeutic activity against cibophobia/lifestyle-related disease, a method for identifying a G protein a subunit and a method of identifying a ligand for SEQ ID NO:2 comprising a screening system as recited in claims 13, 16, 24 and 27 have not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-21, 31-35 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-21, 31-35 and 38 are indefinite because claims recites "therapeutic activity" "lifestyle-related disease" in claims 18, 19, 34, 35 and 38, " activity of the effector" in claims 19, 21 and 32, " activity" in claims 31, 32, 35 and 38. However, Applicant fails to define what "therapeutic activity", "lifestyle-related disease", "activity of

the effector" and " activity" are. Although Applicant provides some examples of the lifestyle-related diseasese in p.4, activity of the effector and effectors in p.34-38, Applicant fails to define/specify what is/is not included within the limitations of the claims. These descriptions are indefinite because there is no limitation on what would or would not be included in a "therapeutic activity", "lifestyle-related disease", " activity of the effector" and " activity" and thus be within the scope of the claims. The disclosure fails to set for the metes and bounds of what is encompassed within the definition of ""therapeutic activity", "lifestyle-related disease", " activity of the effector" and " activity". Thus the artisan would not know what responses Applicant intended to measure.

Statutory Type Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 18-21, 31-35 and 38 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 18-21, 31, 32, 33 and 35 of copending Application No. 10/491654 ('654). The instant claims 18-21, 31-35 and 38 encompass a screening method for a substance having a therapeutic activity against cibophobia or a lifestyle-related disease, comprising adding in each constitution unit of the screening

system comprising a lipid bilayer membrane comprising a polypeptide of SEQ ID NO:2 or modified SEQ ID NO:2 to promote a GDP/GTP exchange reaction of the subunit or a polypeptide comprising at least a receptor-binding region of a G protein α subunit, which are identical to claims 18-21, 31, 32, 33 and 35 of '654. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-21, 31-35 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US20030113798 (effective filing date Dec 12, 2000) in view of Wilson et al. (Br J. Pharmacol. 1998. 125: 1387-1392) and Milligan et al. (Trends Pharmacol. Sci. 1999. 20: 118-24).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

US20030113798 teaches a sequence of G protein-coupled receptor, SEQ ID NO:169, which has 100% identity to the instant SEQ ID NO:2. The sequence search results disclose as follows:

```
US-10-225-567A-619
; Sequence 619, Application US/10225567A
; Publication No. US20030113798A1
; GENERAL INFORMATION:
;  APPLICANT: LifeSpan Biosciences
;  APPLICANT:  Brown, Joseph P.
;  APPLICANT:  Burmer, Glenna C.
;  APPLICANT:  Roush, Christine L.
;  TITLE OF INVENTION: ANTIGENIC PEPTIDES AND ANTIBODIES FOR G PROTEIN-COUPLED
RECEPTORS (GPCRS)
;  FILE REFERENCE: 1920-4-4
;  CURRENT APPLICATION NUMBER: US/10/225,567A
;  CURRENT FILING DATE:  2001-12-19
;  PRIOR APPLICATION NUMBER: 60/257,144
;  PRIOR FILING DATE: 2000-12-19
;  NUMBER OF SEQ ID NOS: 2292
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 619
;   LENGTH: 345
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-225-567A-619

  Query Match             100.0%;  Score 1816;  DB 4;  Length 345;
  Best Local Similarity   100.0%;  Pred. No. 3.2e-154;
  Matches  345;  Conservative   0;  Mismatches   0;  Indels  0;  Gaps  0;

Qy       1 MYKDCIESTGDYFLLCDAEGPWGIILESLAILGIVVTILLLLAFLFLMRKIQDCSQWNVL 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MYKDCIESTGDYFLLCDAEGPWGIILESLAILGIVVTILLLLAFLFLMRKIQDCSQWNVL 60

Qy      61 PTQLLFLLSVLGLFGLAFAFIIELNQQTAPVRYFLFGVLFALCFSCLLLAHASNLVKLVRG 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 PTQLLFLLSVLGLFGLAFAFIIELNQQTAPVRYFLFGVLFALCFSCLLLAHASNLVKLVRG 120

Qy     121 CVSFSWTTILCIAIGCSLLQIIIATEYVTLIMTRGMMFVNMTPCQLNVDFVVLLVYVLFL 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 CVSFSWTTILCIAIGCSLLQIIIATEYVTLIMTRGMMFVNMTPCQLNVDFVVLLVYVLFL 180

Qy     181 MALTFFVSKATFCGPCENWKQHGRLIFITVLFSIIIWVVWISMLLRGNPQFQRQPQWDDP 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 MALTFFVSKATFCGPCENWKQHGRLIFITVLFSIIIWVVWISMLLRGNPQFQRQPQWDDP 240

Qy     241 VVCIALVTNAWVFLLLYIVPELCILYRSCRQECPLQGNACPVTAYQHSFQVENQELSRAR 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 VVCIALVTNAWVFLLLYIVPELCILYRSCRQECPLQGNACPVTAYQHSFQVENQELSRAR 300
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Qy      301 DSDGAEEDVALTSYGTPIQPQTVDPTQECFIPQAKLSPQQDAGGV 345
            ||||||||||||||||||||||||||||||||||||||||||||||
Db      301 DSDGAEEDVALTSYGTPIQPQTVDPTQECFIPQAKLSPQQDAGGV 345
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US20030113798 teaches a method of screening an antibody against SEQ ID NO: 169 (see p.24. Examples 1, 4 and 5). The reference meets the limitation of screening for a substance or a ligand, such as antibody against instant SEQ ID NO:2. But US20030113798 fails to teach a screening system comprising a lipid membrane comprising the polypeptide of SEQ ID NO:2, a G α subunit/polypeptide comprising a receptor-binding region of G α protein, and a polypeptide comprising a guanine nucleotide-binding region and/or an effector.

Wilson et al. teach a reverse molecular pharmacology approach to screen cognate agonists/ligands of orphan GPCR by expressing the orphan GPCR in mammalian cells and screen the cognate agonists/ligands in biological extract preparations, peptide libraries and complex compound collections (p. 1387, abstract). Wilson et al. teach a method of screening ligands/agonists/antagonists by expressing the orphan receptor in a mammalian expression system and measuring the change of intracellular cAMP or Ca levels or phospholipase C (PLC) or by combining with co-expression of G proteins in heterologous GPCR signal pathway, such as promiscuous G-protein $G\alpha_{15/16}$ or chimeric G_q-proteins such as Gqi5. (p. 1389, figure1 and 1st col. to p. 1390 1st col.). The teachings of the screening system comprising a biological extracts comprising the orphan GPCR and measuring the intracellular cAMP/Ca++/PLC and the method of

screening ligands/compounds meet the limitations of the screening systems/methods recited the claims. Wilson et al fail to teach SEQ ID NO:2.

Milligan et al. teach that several chimeric G protein α subunits have been produced and used for screening for potential ligands for G protein-coupled receptors (p. 118, abstract). Milligan et al. teach that several chimeric G proteins using the backbone of G_q, G_i and G_s have been used to screen the agonists/antagonists for example, $G_q\alpha$-$G_{i2}\alpha$ chimera for adenosine A1 receptor and dopamine D2 receptor, C_q-$G_i5\alpha$ chimera for muscarinic acetylcholine M2 receptor or G_s-$G_05\alpha$ for APP (see p. 121, 1st col. to p. 122 the section of Chimeric G protein a subunits and mammalian assay systems)

It would have been obvious for one of ordinary skill in the art at the time of the instant invention was made to combine the teachings of US20030113798, Wilson et al. and Milligan et al. to screen for a potential substance affecting an orphan GPCR, such as GPRC5D/SEQ ID NO:2, or identify a Gα subunit/a ligand responsible for the signal pathway of GPCR5D/SEQ ID NO:2. The person of ordinary skill in the art would have been motivated to incorporate the approaches of manipulating different Gα subunits that are potentially responsible for an orphan receptor and further using the screening system comprising the known Gα subunit responsible for the signal pathway of the specific GPCR, in this case, SEQ ID NO:2 to screen for a potential ligand or substance affecting the signal pathway because it has been shown that the lipid bilayer membrane from biological extract preparation containing potential endogenous cognate ligands

for orphan GPCRs. One of ordinary skill in the art would have expected success in identifying a specific Gα subunit responsible for the signal pathway of GPRC5D/SEQ ID NO:2 or a ligand. Once the potential Gα subunit and ligand are identified, it would be also obvious for one of ordinary skill in the art to screen potential substances known in the art that are able to affect specific Gα subunit in the signal pathway of SEQ ID NO:2.

Conclusion

NO CLAIM IS ALLOWED.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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ABP81722
ID   ABP81722 standard; protein; 345 AA.
AC   ABP81722;
DT   04-MAR-2003  (first entry)
DE   Human G protein-coupled receptor GPRC5D protein SEQ ID NO:619.
KW   G protein-coupled receptor; GPCR; antigenic peptide; gene therapy;
     G protein-coupled receptor modulator; antibody; immune-related disease;
     growth-related disease; cell regeneration-related disease; AIDS; cancer;
     immunological-related cell proliferative disease; autoimmune disease;
     Alzheimer's disease; atherosclerosis; infection; osteoarthritis;
     allergy; osteoporosis; cardiomyopathy; inflammation; Crohn's disease;
     diabetes; graft versus host disease; Parkinson's disease; multiple
     sclerosis; pain; psoriasis; anxiety; depression; schizophrenia;
     dementia; memory loss; mental retardation; epilepsy; asthma;
     tuberculosis; obesity; nausea; hypertension; hypotension; renal
     disorder; rheumatoid arthritis; trauma; ulcer.
OS   Homo sapiens.
PN   WO200261087-A2.
PD   08-AUG-2002.
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PF 19-DEC-2001; 2001WO-US050107.
PR 19-DEC-2000; 2000US-0257144P.
PA (LIFE-) LIFESPAN BIOSCIENCES INC.
PI Burmer GC, Roush CL, Brown JP;
DR WPI; 2003-046718/04.
DR N-PSDB; ABZ42568.
PT New isolated antigenic peptides e.g., for G protein-coupled receptors (GPCR), useful for diagnosing and designing drugs for treating conditions in which GPCRs are involved, e.g. AIDS, Alzheimer's disease, cancer or autoimmune diseases.
PS Disclosure; Fig 1; 523pp; English.
CC The present invention describes antigenic peptides (I) comprising: (a) any one of 1601 sequences (see ABP82019 to ABP83619) of 12-24 amino acids. Also described: (1) an assay for the detection of a particular G protein-coupled receptor (GPCR) or a candidate polypeptide in a sample; and (2) an isolated antibody having high specificity and high affinity or avidity for a particular GPCR. (I) can be used as GPCR modulators and in gene therapy. The antigenic peptides for GPCRs are useful in detecting an antibody against a particular GPCR, and in the production of specific antibodies. The peptides and antibodies are also useful for detecting the presence or absence of corresponding GPCRs. The antigenic peptides for GPCRs and antibodies are useful for diagnosing and designing drugs for treating immune-related diseases, growth-related diseases, cell regeneration-related disease, immunological-related cell proliferative diseases, or autoimmune diseases, e.g. AIDS, Alzheimer's disease, atherosclerosis, bacterial, fungal, protozoan or viral infections, osteoarthritis, osteoporosis, cancer, cardiomyopathy, chronic and acute inflammation, allergies, Crohn's disease, diabetes, graft versus host disease, Parkinson's disease, multiple sclerosis, pain, psoriasis, anxiety, depression, schizophrenia, dementia, mental retardation, memory loss, epilepsy, asthma, tuberculosis, obesity, nausea, hypertension, hypotension, renal disorders, rheumatoid arthritis, trauma, ulcers, or any other disorder in which GPCRs are involved. The antibodies may be used in immunoassays and immunodiagnosis. ABZ42523 to ABZ42869 encode GPCR proteins given in ABP81675 to ABP82018, which are used in the exemplification of the present invention
SQ Sequence 345 AA;

Query Match 100.0%; Score 1816; DB 6; Length 345;
Best Local Similarity 100.0%; Pred. No. 4.2e-181;
Matches 345; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy       1 MYKDCIESTGDYFLLCDAEGPWGIILESLAILGIVVTILLLLAFLFLMRKIQDCSQWNVL 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MYKDCIESTGDYFLLCDAEGPWGIILESLAILGIVVTILLLLAFLFLMRKIQDCSQWNVL 60

Qy      61 PTQLLFLLSVLGLFGLAFAFIIELNQQTAPVRYFLFGVLFALCFSCLLLAHASNLVKLVRG 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 PTQLLFLLSVLGLFGLAFAFIIELNQQTAPVRYFLFGVLFALCFSCLLLAHASNLVKLVRG 120

Qy     121 CVSFSWTTILCIAIGCSLLQIIIATEYVTLIMTRGMMFVNMTPCQLNVDFVVLLVYVLFL 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 CVSFSWTTILCIAIGCSLLQIIIATEYVTLIMTRGMMFVNMTPCQLNVDFVVLLVYVLFL 180
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Qy      181 MALTFFVSKATFCGPCENWKQHGRLIFITVLFSIIIWVVWISMLLRGNPQFQRQPQWDDP 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 MALTFFVSKATFCGPCENWKQHGRLIFITVLFSIIIWVVWISMLLRGNPQFQRQPQWDDP 240

Qy      241 VVCIALVTNAWVFLLLYIVPELCILYRSCRQECPLQGNACPVTAYQHSFQVENQELSRAR 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 VVCIALVTNAWVFLLLYIVPELCILYRSCRQECPLQGNACPVTAYQHSFQVENQELSRAR 300

Qy      301 DSDGAEEDVALTSYGTPIQPQTVDPTQECFIPQAKLSPQQDAGGV 345
            |||||||||||||||||||||||||||||||||||||||||||||
Db      301 DSDGAEEDVALTSYGTPIQPQTVDPTQECFIPQAKLSPQQDAGGV 345
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Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
July 10, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER